IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application No. 10/018,396

Applicant: Cho-Chung

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Mail Stop Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132 OF YOON S. CHO-CHUNG, M.D., PH.D.

I, Yoon S. Cho-Chung, do hereby declare:

- 1. I am the inventor of the subject matter disclosed and claimed in the referenced patent application.
 - 2. The data generated below were generated under my supervision.
- 3. ECPKA activity levels were measured in a variety of cancer cells using the PKA assay disclosed in the subject application (see, e.g., Example 1). The results of this experiment are set forth in Exhibit A. Several different carcinoma cell types were tested, along with three sarcoma cell lines (see e.g., Exhibit A at pages 2 and 4). Normal control cells included PrEC5500 prostate cells and MCF-10A breast cells. ECPKA activity was elevated in each sarcoma sample, as compared to the average ECPKA level of 12.2 mU/ml observed in normal cells.
- 4. The cells used in the experiments referenced above were not engineered to constitutively express ECPKA.

Application No. 10/018,396

Declaration Under 37 C.F.R. § 1.132

5. I hereby declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: MAY 1 2006

Yoon S. Cho-Chung, M.D., Ph.D.

| From Dr. Susan Bate 1-13-2000 (received) | • | | | | | | | | | |
|---|---------------------|------------|--------|----------|------------------|-------|------------------|------|-------|--|
| Samples | | | | | | | | | | |
| No Samples | | (CPM) | | | Mean | | | PKA | | |
| Ca. | I.D. | (-) | | (+) | | | ·(+) | Net | mU/ml | |
| 99 adenocystic | M38502 | 1266 | 1020 | : 512 | 542 | 1143 | 527 | 616 | 40 | |
| 91 bladder | M37629 | 1613 | 1480 | 963 | 675 ² | 1547 | 819 | 728 | 48 | |
| 123 breast adenocarcinom | : M40193 | 1504 | 1666 | 591 | 827 | 1585 | 709 | 876 | 57 | |
| 76 cholangiocarcinoma | M36702 | 867 | 1011 | 557 | 533 | 939 | 545 | 394 | 26 | |
| 20 colon | M32830 | 1488 | 1479 | * 876 | 858 | 1484 | 867 | 617 | 40 | |
| 32 colon | M33708 | 1356 | 1359 | 542 | 511 | 1358 | 527 | 188 | 54 | |
| 37 colon | M34057 | 2194 | 1794 | 1391 | 1407 | 1994 | 1399 | 595 | 39 | |
| 38 colon | M34119 | , 1070 | 984 | 465 | 528 | 1027 | 497 | 531 | 35 | |
| 41 colon | ·M34347 | | | 767 | 726 ¹ | 1152 | 747 | 405 | 26 | |
| 51 colon | M35221 | , 2167 | 2090 | 1060 | 1209 | 2129 | 1135 | 994 | 65 | |
| 53 colon | M35236 | | | | 699 | 1659 | 734 | 926 | 61 | |
| 54 colon | M35362 | 1098 | 1332 | 734 | 898 | 1215 | 816 | 399 | 26 | |
| 58 colon | M35615 | | | | 720 | 2831 | 607 | 2225 | 148 | |
| 59 colon | M35633 | 1446 | 1457 | 588 | 575 | 1452 | 582 | 870 | 57 | |
| 63 colon | M35803 | 1960 | 2044 | 759 | 879 | 2002 | . B19 | 1183 | . 78 | |
| 64 colon | .M35929 | 1663 | 1477 | 694 | 777 | 1570 | 736 | 835 | 55 | |
| 67 colon | M36078 | | | | 610 | 1071 | 672 | 399 | ¦ 26 | |
| 69 colon | M36253 | | | | 756 | 1506 | [:] 785 | 722 | 47 | |
| 74 colon | M36502 | | | | 812 | 1744 | 848 | 896 | 5 59 | |
| 75 colon | M36669 | 2091 | 1938 | 778 | 108 | 2015 | 790 | 1225 | 80 | |
| 77 colon | M36734 | 1291 | 1768 | 845 | 823 | 1530 | 834 | 696 | 45 | |
| 83 colon | M37133 | 1468 | 1451 | 749 | 734 | 1460 | 742 | 718 | 47 | |
| 88 colon | :M37506 | 1523 | 1825 | 554 | 543 | 1674 | 549 | 1126 | 74 | |
| 98 colon | M38428 | 1779 | 1929 | 745 | 741 | 1854 | 743 | 1111 | 73 | |
| 103 colon | ¹ M38696 | 1057 | 891 | 542 | 542 | 974 | 542 | 432 | 28 | |
| 106 colon | M33925 | | | 754 | 865 [;] | 2229 | 810 | 1420 | 93 | |
| 109 colon | M39044 | 1386 | 1803 | 702 | 745 | 1595 | 724 | 871 | 57 | |
| 116 colon | M39491 | | • | | 648 | 1732 | 630 | 1102 | . 72 | |
| 118 colon | M39752 | 1677 | 1487 | , | 714 | 1.582 | 2 709 | 874 | 5 | |
| 135 colon | M41110 | 1780 | ; 1369 | 465 | 668 | 1575 | 5 567 | 1008 | 66 | |
| 137 colon | M41249 | 1932 | 1288 | 794 | 746 | 1610 | - | | 55 | |
| 135 colon | _i M41110 | | | | 668 | 1575 | | | | |
| 137 colon | M41249 | 1932 | 1288 | 794 | 746 | | | | | |
| 125 gastric adenocarcino | | | | | 536 | 122 | 1 524 | 697 | 46 | |

| 12 hepatoblastoma | M31946 1326 1321 | | | 1204 | | 510 | 24.0 |
|--------------------|--------------------------------------|------------------|--------------------------|------|------------------|------------------|------|
| , | 1320 1321 | 781 | 828 | 1324 | 805 | 519 | 34.3 |
| 52 hepatocellular | M35234 1591 1838 | 629 | 653 | 1715 | 641 | 1074 | 70.9 |
| 94, leiomyosarcoma | M37702 1543 1542 | 618 | 682. | 1543 | 650 | 893 | 58.9 |
| 31 liposarcoma | M33702 1773 1429 | 706 | 727 | 1601 | 717 | 885 | 58.4 |
| 1 lung | M27795 1639 1310 | 897 | 784 | 1475 | 841 | 634 | 41.9 |
| 10 lung | M31464 1749 1372 | 777. | 790 | 1561 | 784 | 777 | 51.3 |
| 46 lung | M34780 1784 _: 1777 | 600 | 626 | 1781 | 613 | 1168 | 77.1 |
| 57 lung | M35511 1167 1464 | 777 | 822 | 1316 | 800 | 516 | 34,1 |
| 68 lung | M35155 1334 1401 | 713 | 739 | 1368 | 726 | 642 | 42.4 |
| 87 lung | M37434 2407 1803 | 837 | 983 | 2105 | 910 | 1195 | 78.9 |
| 62 lymphoma | M35760 1070 1450 | 745 | 644 | 1260 | 695 | 566 | 37.3 |
| 2 melanoma | M30538 1393, 1652 | 830 | 732 | 1523 | 781 | 742 | 49.0 |
| 3 melanoma | M30625 2080, 1720, | 840 | 923 | 1900 | 882 | 1019 | 67.2 |
| 4 melanoma | M30848 1319 1423 | 712 | 704, | 1371 | 708 | 663 | 43.8 |
| 6 melanoma | M31230 2109 1771 | 721 | 960 | 1940 | 841 | 1100 | 72.6 |
| 7 melanoma | M31342 _{1405 1232} | 687 | 7 30 ⁻ | 1319 | 709 | 610 | 40.3 |
| 8 melanoma | M31360 ₁₈₄₃ 1601 | 864 | B3B | 1722 | 851 | 871 | 57.5 |
| 13 melanoma | M32115 1956 1766 | 899 | 844 | 1861 | 872 | 990 | 65.3 |
| 14 melanoma | M32142 _{1945 2041} | 950 | 1036 | 1993 | 993 | 1000 | 66.0 |
| 16 melanoma | M32170 1934 1532 | 789 [°] | 706 | 1733 | 748 | 986 | 65.1 |
| 17 melanoma | M32235 1749 1415 | 783 | 727 | 1582 | 755 [:] | 827 | 54.6 |
| 18 melanoma | M32448 2316 2362 | 1044 | 1028 | 2339 | 1036 | 1303 | 0.88 |
| 19 melanoma | M32535 1748, 2322 | 1054 | 965 | 2035 | 1010 | 1026 | 67.7 |
| 22 melanoma | M32936 1518 1516 | 812 | 744 | 1517 | 778 | 739 | 48.8 |
| 23 melanoma | M32942 1490 1544 | 826 | 823 | 1517 | 825 | 693 | 45.7 |
| 24 melanoma | M33031 1338 1463 | 986 | 794 | 1401 | 890 | 511 | 33.7 |
| 25 melanoma | M33090 1465 1330 | 705 | 863 | 1398 | 784 | 614 | 40.5 |
| 26 melanoma | M33092 1667 1674 | 743 | 745 [!] | 1671 | 744 | 927 | 61.2 |
| 27 melanoma | M33178 1916 1845 | 915 | 924 | 1881 | 920 | 961 | 63.4 |
| 34 melanoma | :M33957 1418 1246 | 688 | 619 | 1332 | 654 | 679 | 44.8 |
| 35 melanoma | M33987 1633 1552 | 807. | 672 | 1593 | 740 | 853 [°] | 56.3 |
| 40 melanoma | M34338 1753 1610 | 822 | 764 | 1682 | 793 | 889 | 58.7 |
| 44 melanoma | <u> </u> | 685 | 779 | 1783 | 732 | 1051 | 69.4 |
| 48 melanoma | M34710 1748 1818 M34977 1432 1772 | 679 | | 1602 | 649 | 954 | 62.9 |
| k : | M35027 1284 1100 | | 618 | 1192 | 769 | 423 | 27.9 |
| 50 melanoma | | 701 550 | 837 920 | 1218 | 690 | 528 | i |
| 56 melanoma | M35482 1269 1166 | 559 | 820 | 1496 | 838 | 659 | 34.9 |
| 65 melanoma | M36042 1518 1474 | 783 | 892, | 1493 | 964 ¹ | | 43.5 |
| 71 melanoma | M36363 1332 1653 | 925 | 1003 | : | - i | 529 | 34.9 |
| 80 melanoma | M36963 1500 1595 | 731 | 890 | 1548 | 811 | 737 | 48.7 |
| 82 melanoma | .M37072 1717, 1714, | 912 | 857 | 1716 | 885 | 831 | 54.9 |

| 90 melanoma | M37621 1906 2097 | 927 | 1068 | 2002 | 998 | 1004 | 66.3 |
|-----------------------------------|--------------------|--------------|------------------|-------|-------|--------------|--------------|
| 92 melanoma | M37649 1588 1309. | 734 | 963 | 1449 | 849 | 600 | 39.6 |
| 95 melanoma | M37877 921 1157 | 462 | 521 | 1039 | 492 | 548 | 36.1 |
| 96 melanoma | M38072 1168, 1330 | 926 | 711 | 1249 | 819 | 431 | 28.4 |
| 105 melanoma | M38706 1473 1227 | 512 | 542 | 1350 | , 527 | 823 | 54.3 |
| 107 melanoma | M38940 1354 1616 | 645 | 685 | 1485 | 665 | 820 | 54.1 |
| 108 melanoma | M33978 1999 2301 | 765 | 812 | 2150 | 789 | 1362 | 89.9 |
| 112 melanoma | M39083 1404 1474 | 712 | 732 | 1439 | 722 | 717 | 47.3 |
| 115 melanoma | M39412 2185 2010 | 912 | 942 | 2098 | 927 | 1171 | 77,3 |
| 126 melanoma | M40340 1490 1537 | 477. | 494 | 1514 | 486 | 1028 | 67.9 |
| 130 melanoma | M40898 2221 2034 | 643 | 760 | 2128 | 702 | 1426 | 94.1 |
| .34 melanoma | M41094 1212 1113 | 522 | 414 | 1163 | 468 | 695 | 45.9 |
| 136 melanoma | M41123 2233 2901 | 700 | 565 [°] | 2567 | 633 | 1935 | 127.7 |
| 138 melanoma | M41360 1271 1134. | 593 , | 475 | 1203 | 534 | 669 | 44.1 |
| 130 melanoma | M40898 2221 2034 | 643 | 760 | 2128 | 702 | 1426 | 94.1 |
| 134 melanoma | .M41094 1212 1113 | 522 | 414 | 1163 | 468 | 695 | 45.9 |
| 136 melanoma | M41123 2233 2901 | 700 | 565 | 2567 | 633 | 1935 | 127.7 |
| 138 melanoma | M41360 1271 1134. | 593 | 475 | 1203 | 534 | 669 | 44.1 |
| 9 ovarian | M31393 1472 1595 | 902 | 754 | 1534 | 828 | 706 . | 46.6 |
| 117 ovarian | M39616 1933 1352 | 645 | 614 | 1643 | 630 | 1013 | 66.9 |
| 124 ovarian adenocarcino | • • | 628 | 502 | 1499 | 565 | 934 | 61.6 |
| 11 pancreatic | M31787 · 1509 1578 | 724 | 713 | 1544 | 719 | 825 | 54.5 |
| 73 pancreatic | M36494 1462 1243 | 573 | 648 | 1353 | 611 | 742 | 49.0 |
| 86 pancreatic | M37418 1243 1137 | B09 | 632 | 1190 | 721 | 470 | 31.0 |
| 30 pnacreatic | M33489 1916 1930 | 775 | 935 | 1923 | 855 | 1068 | 70.5 |
| 43 rectal | M34573 1302 1247 | 625 | 588 | 1275 | 607 | 668 | 44.1 |
| 47 rectal | M34868 1445 1196 | 685 | 634 | 1321 | 660 | 661 | 43,6 |
| 72 rectal | M36437 1537 1782 | 869 | 767 | 1660 | 818 | 842 | 55.6 |
| | M37576 1735 2126 | 940 | 827, | 1931 | 884 | 1047 | 69.1 |
| 89 rectal | M41374 876 856 | 495 | 424 | 866 | 460 | 407 | 26.8 |
| 139 rectal | M41374 876 856 | 495 | 424 | 866 | 460 | 407 | 26.8 |
| 139 rectal 5 renal cell carcinoma | M30974 1724 1990 | 687. | 911 | 1857 | 799 | 1058 | 69.8 |
| 21 renal cell carcinoma | · • | • | 747 | 1514 | 746 | 768 | 50.7 |
| 28 renal cell carcinoma | M32912 1605 1422 | 745 | | 1665 | 753 | 912 | 60.2 |
| 29 renal cell carcinoma | M33297 1590 1739 | 704 | 802 | 1938 | 779. | 1160 | |
| 33 renal cell carcinoma | M33403 1979 1897 | 768 | 789 _i | 1611 | 709 | 903 | 76.5 59.6 |
| 36 renal cell carcinoma | M33927 1514 1708 | 759; | 65B | 1845 | 856 | 989 | |
| | • | 855; | 856 | 1447. | 688 | 759 | 65.3 |
| 39 renal cell carcinoma | | 738 | 637 | | | | 50.1 |
| 42 renal cell carcinoma | | 629 | 820 | 1529 | 725 | 805 | 53.1 |
| 45 renal cell carcinoma | M34749 1468 1885 | 872 | 779 | 1677 | 826 | 851 | 56.2 |

| | · | | | #500 | 0.00 | 922 | 54.0 |
|--------------------------|----------------------|------------------|------------------|-------|------------------|------|-------|
| 49 renal cell carcinoma | M35022 1885 1698 | 1001 | 936 | 1792 | 969 | 823 | 54.3 |
| 55 renal cell carcinoma | M35380 1745 1931 | 969. | 833. | 183B | 901 | 937 | 61.9 |
| 60 renal cell carcinoma | M35658 2251 2426 | 791 _i | 746. | 2339 | 769 | 1570 | 103.7 |
| 61 renal cell carcinoma | M35713 1492 · 1546 | 888 | 955 | 1519 | 922 | 598 | 39.4 |
| 66 renal cell carcinoma | M36060 1488 1307 | 933 | 939 | 1398 | 936 | 462 | 30.5 |
| 70 renal cell carcinoma | M36330 2800 2483 | 867 | 749 | 2642 | 808 | 1834 | 121.0 |
| 78 renal cell carcinoma | M36787 1589 1540 | 904 | 756 | 1565 | 830 | 735 | 48.5 |
| 79 renal cell carcinoma | M36812 2011 1660 | 710 _. | 658 | 1836 | б84 | 1152 | 76.0 |
| 81 renal cell carcinoma | M37050 1519 1453 | 848 | 578 | 1486 | 713 | 773 | 51.0 |
| 84 renal cell carcinoma | M37274 1402 1177 | 742 | 512 | 1290 | 627 | 663 | 43.7 |
| 85 renal cell carcinoma | M37361 1317 1586 | 654 | 621 | 1452 | 638 | 814 | 53.7 |
| 93 renal cell carcinoma | M37660 1501 1665 | 660 | 799 | 1583 | 730 | 854 | 56.3 |
| 97 renal cell carcinoma | M38334 1582 1578 | 602 | 645 | 1580 | 624 | 957 | 63.1 |
| 100 renal cell carcinoma | M38564 1882 1560 | 621 | 645 [†] | 1721 | 633 | 1088 | 71.B |
| 101 renal cell carcinoma | M38585 1478 1206 | 542 | 561 | 1342 | 552 | 791 | 52.2 |
| 102 renal cell carcinoma | | 745 | 748 | 1886 | 747 | 1140 | 75.2 |
| 104 renal cell carcinoma | | 451 | 462 | 1295 | 457 | 838 | 55.3 |
| 110 renal cell carcinoma | | 856 | 912 | 2614 | 884 | 1730 | 114.2 |
| 111 renal cell carcinoma | M39067 1428 1343 | 645 | 668 | 1386 | 657 | 729 | 48.1 |
| 113 renal cell carcinoma | | 912 | 912 _i | 1939 | 912 | 1027 | 67.8 |
| 114 renal cell carcinoma | M39305 2125 2311 | 984 | 912 | 2218 | 948 | 1270 | 83.8 |
| 119 renal cell carcinoma | M39884 1639 1232 | 465 | 485 | 1436 | 475 | 961 | 63.4 |
| 120 renal cell carcinoma | M39921 1957: 1799 | 703 [!] | 712 | 1878 | 708 | 1171 | 77.3 |
| 121 renal cell carcinoma | M39939 1228 1145 | 642 | 728 | 1187 | 685 | 502 | 33.1 |
| 122 renal cell carcinoma | M40045 2018 1856, | 583 | 700 | 1937 | 642 | 1296 | 85.5 |
| 128 renal cell carcinoma | M40696 1554 1542 | 670 | 728 | 1548 | 699 . | 849 | 56.1 |
| 129 renal cell carcinoma | M40705 1659 1671 | 620 | 637 | 1665 | 629 | 1037 | 68.4 |
| 132 renal cell carcinoma | M41054 1457 1502 | 499 | 564 | 1480 | 532 | 948 | 62.6 |
| 133 renal cell carcinoma | M41079 1133 1054 | 778 | 648 . | 1094 | 713 | 381 | 25.1 |
| 140 renal cell carcinoma | M41421 2555 2659 | 795 | 691 | 2607 | 743, | 1864 | 123.1 |
| 129 renal cell carcinoma | M40705 1659 1671 | 620 | 637 [°] | 1665 | 629 | 1037 | 68.4 |
| 132 renal cell carcinoma | M41054 1457 1502 | 499 | 564 | 1480 | 532 | 948 | 62.6 |
| 133 renal cell carcinoma | M41079 1133 1054 | 778 | 648 | 1094 | 713 | 381 | 25.1 |
| 140 renal cell carcinoma | M41421 2555 2659 | 795 [!] | 691 | 2607 | 743 | 1864 | 123.1 |
| 127 sarcoma | :M40404 1024 947, | 571 | 550 . | 986 | 561 ⁱ | 425 | 28.1 |
| 131 synorial cell | M40909 2073 2503 | 786 i | 816 | 2288 | 801 _! | 1487 | 98.2 |
| 131 synorial cell | M40909 2073 2503 | 786 | 816 | 2288, | 801 | 1487 | 98.2 |
| 15 thymoma | M32165 . 1598 1512 | 945 | 806. | 1555 | 876 | 680 | 44.9 |
| | | <u> </u> | | | | | |